

POSTER PRESENTATION

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Naive CD8⁺ T cells from ART respond to primary vaccination against autologous HIV-1 antigen

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Introduction

Antiretroviral therapy (ART) decreases HIV-1 viremia and AIDS-associated mortality. Despite this, HIV infected patients are unable to clear virus during treatment interruption due to insufficient cytotoxic T cell (CTL) activity against the autologous reservoir. It is unclear if naïve T cells from patients on ART can respond to immunotherapies that induce CTL specific for their own, unique virus. Unfortunately, late-evolving virus and the ART reservoir contain escape epitope variants that confer a lack of CTL control. We hypothesize that a dendritic cell (DC)-based immunotherapy during ART can induce CTL capable of eliminating the autologous reservoir, despite their failure to do so during natural infection.

Materials and methods

We use a naïve T cell flow cytometry panel to evaluate changes in the naïve CD4⁺:CD8⁺ T cell ratio before seroconversion, during untreated infection, and after ART in an HIV infected subject. We then use this panel to isolate naïve CD4⁺ and CD8⁺ T cells from this patient during ART and from HIV negative donors. These purified naïve T cells are then used in an in vitro model of dendritic cell (DC) vaccination at their in vivo ratios to induce primary IFN γ -producing CTL against autologous HIV-1 Gag, Env, and Nef peptide antigens derived from ART.

Results

Although partial immune reconstitution occurs during ART, we observed a disproportionate recovery in the naïve CD4⁺:CD8⁺ T cell ratio compared to pre-infection. Despite this, we show that naïve CD4⁺ and CD8⁺ T cells from ART, when primed at their skewed in vivo

ratio against late-acquired, “escape” epitope variants, differentiate into IFN γ -producing CTL comparable to those induced in pre-seroconversion T cells. Additionally, we show that primary CTL responses induced during ART are comparable to those observed in HIV negative donors. Figure 1.

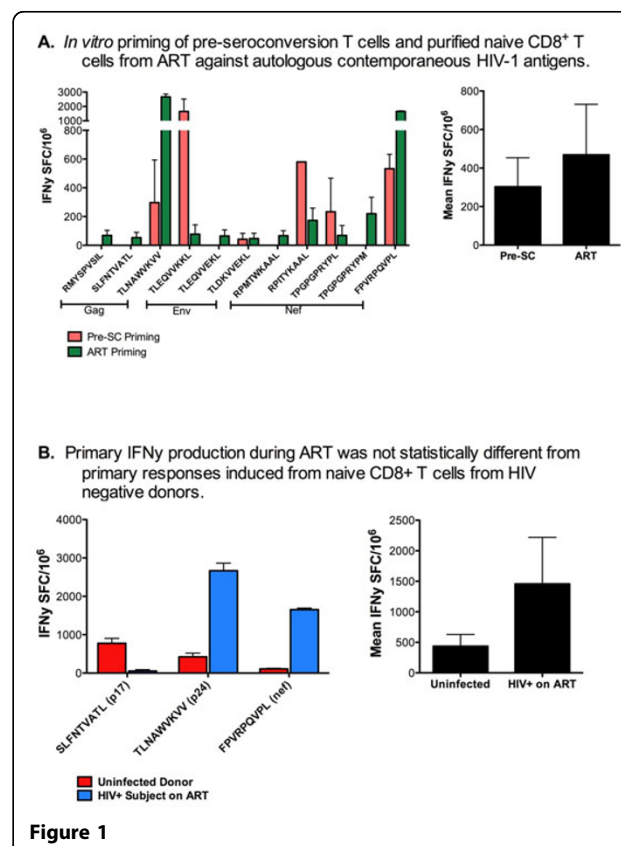


Figure 1

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Conclusion

These data indicate that, despite a disproportionate recovery in the naïve CD4+:CD8+ T cell ratio, DC vaccination of naïve T cells from ART can induce CTL specific for autologous “escape” HIV-1 variants, and that these naïve T cells can respond to primary vaccination at a level similar to pre-infection. These data support the use of DC immunotherapies in HIV infected patients on ART.

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